

**Study Number:** C11049-01

**Test Type:** TOX

**Route:** Nose-Only Inhalation

**Species/Strain:** Rat/Harlan Sprague Dawley

**Study Number:**

**Study Gender:**

**PWG Approval Date:**

**PA10X: Statistical Analysis of Non-Neoplastic Lesions**

**Test Compound:** Trimethylsilyldiazomethane

**CAS Number:** 18107-18-1

C11049-01

Male

See web page for date of PWG Approval

**Date Report Requested:** 10/22/2020

**Time Report Requested:** 09:33:45

**Lab:** Battelle with CRL

Study Number: C11049-01

Test Type: TOX

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Species/Strain: Rat/Harlan Sprague Dawley

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Test Compound: Trimethylsilyldiazomethane

CAS Number: 18107-18-1

Date Report Requested: 10/22/2020

Time Report Requested: 09:33:45

Lab: Battelle with CRL

Male : 1 Day Exposure

Treatment Groups (ppm)

	0	10	25 ppm Hexanes
<b>Disposition Summary</b>			
Animals Initially In Study	8	8	8
Early Deaths			
Scheduled Deaths			
Scheduled sacrifice, terminal (SD 1)	8	8	8
Number of Animals Examined	8	8	8
<b>ALIMENTARY SYSTEM</b>			
LIVER	(8)	(8)	(8)
HEMATOPOIETIC CELL PROLIFERATION		1 (12.5%)	
PHARYNX	(8)	(8)	(8)
HYPERPLASIA; SQUAMOUS		1 (12.5%)	
<b>CARDIOVASCULAR SYSTEM</b>			
None			
<b>ENDOCRINE SYSTEM</b>			
None			
<b>GENERAL BODY SYSTEM</b>			
None			
<b>GENITAL SYSTEM</b>			
None			
<b>HEMATOLYMPHOID SYSTEM</b>			
None			
<b>INTEGUMENTARY SYSTEM</b>			
None			

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Lab: Battelle with CRL

Male : 1 Day Exposure

Treatment Groups (ppm)

0

10

25 ppm Hexanes

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

LARYNX	(7)	(8)	(8)
EPIGLOTTIS; INFLAMMATION		1 (12.5%)	
INFLAMMATION; CHRONIC-ACTIVE	1 (14.3%)		
EPIGLOTTIS; METAPLASIA; SQUAMOUS		1 (12.5%)	
LUNG	(8)	(8)	(8)
ERYTHROPHAGOCYTOSIS		1 (12.5%)	
HEMORRHAGE; ACUTE	1 (12.5%)	1 (12.5%)	
INFILTRATION, CELLULAR; MIXED		1 (12.5%)	
TRACHEA	(8)	(8)	(8)
EPITHELIUM; DEGENERATION		1 (12.5%)	

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

KIDNEY, LEFT	(8)	(8)	(8)
INFILTRATE, CELLULAR; MIXED		1 (12.5%)	2 (25%)
NEPHROPATHY	2 (25%)	3 (37.5%)	1 (12.5%)

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Lab: Battelle with CRL

Male : 1 Day Recovery

	Treatment Groups (ppm)		
	0	10	25 ppm Hexanes
<b>Disposition Summary</b>			
Animals Initially In Study	8	8	8
Early Deaths			
Scheduled Deaths			
Scheduled sacrifice, terminal (SD 9)	8	8	8
Number of Animals Examined	8	8	8
<b>ALIMENTARY SYSTEM</b>			
LIVER	(8)	(8)	(8)
CLEAR CELL FOCUS		1 (12.5%)	
HEMATOPOIETIC CELL PROLIFERATION			1 (12.5%)
HEPATODIAPHRAGMATIC NODULE	1 (12.5%)		
<b>CARDIOVASCULAR SYSTEM</b>			
None			
<b>ENDOCRINE SYSTEM</b>			
None			
<b>GENERAL BODY SYSTEM</b>			
None			
<b>GENITAL SYSTEM</b>			
None			
<b>HEMATOLYMPHOID SYSTEM</b>			
None			
<b>INTEGUMENTARY SYSTEM</b>			
None			

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Male : 1 Day Recovery

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Treatment Groups (ppm)

---

0

10

25 ppm Hexanes

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**MUSCULOSKELETAL SYSTEM**

None

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**NERVOUS SYSTEM**

None

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**RESPIRATORY SYSTEM**

LUNG

(8)

(8)

(8)

HEMORRHAGE; ACUTE

1 (12.5%)

PERIVASCULAR; INFILTRATION, CELLULAR; MIXED

2 (25%)

NOSE

(8)

(8)

(8)

GOBLET CELL; HYPERPLASIA

1 (12.5%)

INFLAMMATION; LYMPHOHISTIOCYTIC

1 (12.5%)

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**SPECIAL SENSES SYSTEM**

None

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**URINARY SYSTEM**

KIDNEY, LEFT

(8)

(8)

(8)

NEPHROPATHY

7 (87.5%)

3 (37.5%)

3 (37.5%)

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Lab: Battelle with CRL

Male : 5 Day Exposure

	Treatment Groups (ppm)					
	0	0.3	1	3	10	25 ppm Hexanes
<b>Disposition Summary</b>						
Animals Initially In Study	8	8	8	8	8	8
Early Deaths						
Scheduled Deaths						
Scheduled sacrifice, terminal (SD 5)	8	8	8	8	8	8
Number of Animals Examined	8		8	8	8	8
<b>ALIMENTARY SYSTEM</b>						
LIVER	(8)	(0)	(0)	(0)	(8)	(8)
HEMATOPOIETIC CELL PROLIFERATION					1 (12.5%)	1 (12.5%)
<b>CARDIOVASCULAR SYSTEM</b>						
None						
<b>ENDOCRINE SYSTEM</b>						
None						
<b>GENERAL BODY SYSTEM</b>						
None						
<b>GENITAL SYSTEM</b>						
None						
<b>HEMATOLYMPHOID SYSTEM</b>						
LYMPH NODE, MEDIASTINAL	(8)	(0)	(7)	(8)	(8)	(8)
LYMPHOID TISSUE; HYPERPLASIA			2 (28.6%)			1 (12.5%)
INFILTRATION, CELLULAR; HISTIOCYTE	0 **			1 (12.5%)	8 (100%) **	2 (25%)
<b>INTEGUMENTARY SYSTEM</b>						
None						

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Test Type: TOX

Route: Nose-Only Inhalation

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Lab: Battelle with CRL

Male : 5 Day Exposure

Treatment Groups (ppm)

0 0.3 1 3 10 25 ppm Hexanes

MUSCULOSKELETAL SYSTEM

None

NERVOUS SYSTEM

None

RESPIRATORY SYSTEM

LARYNX	(8)	(0)	(0)	(0)	(8)	(8)
EPITHELIAL CELL; HYPERPLASIA; SQUAMOUS					2 (25%)	
EPIGLOTTIS; METAPLASIA; SQUAMOUS					2 (25%)	
LUNG	(8)	(0)	(8)	(8)	(8)	(8)
EDEMA	0 **				7 (87.5%) **	
INTERSTITIUM; FIBROSIS	0 **				8 (100%) **	
HEMORRHAGE; ACUTE	0 **				8 (100%) **	
ALVEOLAR EPITHELIUM; HYPERPLASIA	0 **			6 (75%) **	8 (100%) **	
BRONCHIOLE EPITHELIUM; HYPERPLASIA	0 **			7 (87.5%) **	8 (100%) **	
INFILTRATION, CELLULAR; HISTIOCYTE				7 (87.5%) **		
INFLAMMATION; CHRONIC-ACTIVE	0 **			7 (87.5%) **	8 (100%) **	
INFLAMMATION; CHRONIC-ACTIVE, FOCAL			2 (25%)			
TRACHEA	(8)	(0)	(0)	(0)	(8)	(8)
EPITHELIUM; DEGENERATION						1 (12.5%)

SPECIAL SENSES SYSTEM

None

URINARY SYSTEM

KIDNEY, LEFT	(8)	(0)	(0)	(0)	(8)	(8)
NEPHROPATHY	3 (37.5%)					2 (25%)

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Lab: Battelle with CRL

Male : 5 Day Recovery

	Treatment Groups (ppm)					
	0	0.3	1	3	10	25 ppm Hexanes
<b>Disposition Summary</b>						
Animals Initially In Study	8	8	8	8	8	8
Early Deaths						
Scheduled Deaths						
Scheduled sacrifice, terminal (SD 9)	8	8	8	8	8	8
Number of Animals Examined	8	8	8	8	8	8
<b>ALIMENTARY SYSTEM</b>						
None						
<b>CARDIOVASCULAR SYSTEM</b>						
None						
<b>ENDOCRINE SYSTEM</b>						
None						
<b>GENERAL BODY SYSTEM</b>						
None						
<b>GENITAL SYSTEM</b>						
None						
<b>HEMATOLYMPHOID SYSTEM</b>						
LYMPH NODE, MEDIASTINAL	(8)	(0)	(8)	(8)	(8)	(8)
LYMPHOID TISSUE; HYPERPLASIA	1 (12.5%)		2 (25%)	2 (25%)	2 (25%)	1 (12.5%)
INFILTRATION, CELLULAR; HISTIOCYTE	1 (12.5%) **			5 (62.5%)	8 (100%) **	
<b>INTEGUMENTARY SYSTEM</b>						
None						

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Lab: Battelle with CRL

Male : 5 Day Recovery

	Treatment Groups (ppm)					
	0	0.3	1	3	10	25 ppm Hexanes
<b>MUSCULOSKELETAL SYSTEM</b>						
None						
<b>NERVOUS SYSTEM</b>						
None						
<b>RESPIRATORY SYSTEM</b>						
LARYNX	(8)	(0)	(0)	(0)	(8)	(8)
INFILTRATION, CELLULAR; MIXED						2 (25%)
LUNG	(8)	(8)	(8)	(8)	(8)	(8)
EDEMA	0 **				7 (87.5%) **	
INTERSTITIUM; FIBROSIS	0 **				8 (100%) **	
HEMORRHAGE; ACUTE	0 **	1 (12.5%)	1 (12.5%)	3 (37.5%)	8 (100%) **	
ALVEOLAR EPITHELIUM; HYPERPLASIA	0 **		1 (12.5%)	2 (25%)	8 (100%) **	
BRONCHIOLE EPITHELIUM; HYPERPLASIA	0 **				6 (75%) **	
INFILTRATION, CELLULAR; HISTIOCYTE		1 (12.5%)	2 (25%)	8 (100%) **		
INFLAMMATION; CHRONIC-ACTIVE	0 **		2 (25%)	8 (100%) **	8 (100%) **	
INFLAMMATION; CHRONIC-ACTIVE, FOCAL	1 (12.5%)	3 (37.5%)				1 (12.5%)
NOSE	(8)	(0)	(0)	(0)	(8)	(8)
INFILTRATION, CELLULAR; NEUTROPHIL					2 (25%)	
INFLAMMATION; CHRONIC						1 (12.5%)
TRACHEA	(8)	(0)	(0)	(0)	(8)	(8)
EPITHELIUM; DEGENERATION					1 (12.5%)	
<b>SPECIAL SENSES SYSTEM</b>						
None						
<b>URINARY SYSTEM</b>						
KIDNEY, LEFT	(8)	(0)	(0)	(0)	(8)	(8)
NEPHROPATHY	2 (25%)				6 (75%)	1 (12.5%)

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## LEGEND

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Number of animals examined for each tissue shown in parentheses. If none of the animals examined have the specific lesion then there is a blank for that dose group for that specific lesion. The exception to this is if statistical significance is found for a lesion and the control group has no animals with the lesion then a 0 is included for the control group on the table for that lesion.

Number of animals with observation reported with percent incidence in parentheses

Statistical analysis performed by Cochran-Armitage (trend) and Fisher Exact (pairwise) tests.

Statistical analysis for the negative control group compared to the vehicle control group was performed using the Fisher Exact test.

Trend significance is reported only for those organs that were fully examined in the control group plus two or more other dose groups. For organs that were fully examined in just the control and one other dose group, only the pairwise significance is reported.

Statistical significance for the control group indicates a significant trend test

Statistical significance for a treatment group indicates a significant pairwise test compared to the vehicle control group

All trend and pairwise p-values are reported as one-sided.

\* Statistically significant at  $P \leq 0.05$

\*\* Statistically significant at  $P \leq 0.01$

The 1 Day Exposure animals were exposed for one day and then sacrificed on study day 1 (first day of exposure was study day 0); the 1 Day Recovery animals were exposed for 1 day and then sacrificed on study day 9; the 5 Day Exposure animals were exposed for five days and then sacrificed on study day 5; the 5 Day Recovery animals were exposed for five days and then sacrificed on study day 9.

**\*\* END OF REPORT \*\***